PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Rec'd PCT/PTO 12 JUL 2004

Applicant's or agent's file reference 27.14.77359/002	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/00156	International filing date *(day/month/year)* 16.01.2003	Priority date *(day/month/year)* 16.01.2002
International Patent Classification (IPC) or both national classification and IPC C12Q1/68, C12Q1		
Applicant DYNAL BIOTECH ASA et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06.06.2003	17.02.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Tilkorn, A-C Telephone No. +49 89 2399-8688

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/00156

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-53 as originally filed

Claims, Numbers

1-33 received on 27.01.2004 with letter of 26.01.2004

Drawings, Sheets

1/14-14/14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-33
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-33
Industrial applicability (IA)	Yes:	Claims	1-33
	No:	Claims	-

2. Citations and explanations

see separate sheet

Re Item V

The following documents are referred to in this communication:

D1: WO 00 61806 A
D2: Nucleic Acids Research (1998) **26(21)** 5007-5008
D3: DE 4237381 C
D4: EP 0 885 958 A

1 Novelty (Art 33(2) PCT):

1.1 **Claims 1-29, 33** are novel, because none of the available documents discloses a method involving isolating nucleic acid and protein from the same sample wherein nucleic acid and protein are bound to distinct solid supports.

1.2 Similarly, **claims 30-32** are novel, because none of the available documents discloses a kit comprising distinct solid supports for binding nucleic acid components and proteins, respectively.

2 Inventive Step (Art 33(3) PCT):

2.1 **Claim 1** is not inventive over D1, which is considered to represent the closest prior art:
D1 discloses the simultaneous detection of HER-2/neu mRNA and protein (Example 2).
Claim 1 is distinguished from the method of D1 in that it requires that nucleic acid and protein components of the same sample become bound to distinct solid supports, whereas according to D1 nucleic acid and protein become bound to different areas of the same solid support.
The difference between the subject-matter of claim 1 and D1 seems to be a matter of design and does not appear to solve a technical problem. Even the present application envisages to provide distinct solid supports as different areas of the same solid support (see application: page 13 line 23-25). Moreover, the skilled person who is interested in further processing of the isolated nucleic acid or protein, is aware of ways to separate different areas of a solid support without using inventive skill.

Thus, inventiveness cannot be acknowledged. Moreover, a design as defined in claim 1 is used in the method of D2 (Fig. 1). As the further features contained in dependent **claims 2-29** do not seem to be based on an inventive idea but belong to the standard repertoire of the skilled person (e.g. binding of mRNA to a support by using oligo dT cf. D4: col 11 line 29-38) , said claims are not considered inventive, either.

2.2 **Claim 30** does not seem to be inventive for the following reasons: The skilled person who wants to economically exploit the method of D2 (abstract, page 5007 col 1 para 3- col 2 para 1, Figure 1) would put together a kit comprising said two solid supports (D2: page 5007 col 1 para 3- col 2 para 1). The kit according to claim 30 does not appear to be inventive over said kit on the basis of the method of D2 (abstract, Figure 1, page 5008 col 1 para 2-col 2 par 1). The same argument applies to the kits defined in **claims 31** and **32.**

2.3 **Claim 33** is directed to the use of the method of claim 1, which is also envisaged in D1 (D1: page 2 para 2-4, page 17 para 5). Thus, **claim 33** contravenes Art 33(3) PCT.

3 Clarity/Support (Art 6 PCT):

3.1 **Claims 30-32** contravene Art 6 PCT, because the scope of the claims as defined by the functional definition "suitable for binding nucleic acids/proteins" is not commensurate with the contribution of the application to the art.

3.2 **Claim 33** infringes Art 6 PCT, because its category is not clear: The claim pertains to the use of a method; however, claims 30-32 are directed to a kit.

77359/002.623

Claims

1. A method of isolating nucleic acid and protein from the same sample, said method comprising contacting said sample with solid supports, wherein nucleic acid and protein components contained in said sample become bound to distinct solid supports.

2. The method of claim 1, wherein both DNA and RNA are bound to the same solid support.

3. The method of claim 1, wherein DNA and RNA are bound to distinct solid supports.

4. The method of claim 3, wherein DNA and RNA are bound to different solid supports in separate steps.

5. The method of any one of claims 1 to 4, wherein RNA and protein, or DNA and protein, or DNA, RNA and protein are isolated from the same sample.

6. The method of claim 5, wherein said RNA is mRNA.

7. The method of claim 5 or 6, wherein said DNA is genomic.

8. The method of any one of claims 1 to 7 wherein the total RNA and/or the total DNA is isolated.

9. The method of any one of claims 1 to 7 wherein the total nucleic acid component is isolated.

10. The method of any one of claims 1 to 9 wherein the total protein component is isolated.

11. The method of any one of claims 1 to 10, wherein said sample is a food or allied product, or is a clinical, environmental or biological sample.

12. The method of any one of claims 1 to 11, wherein prior to contacting said sample with said solid supports, the sample is subjected to a preliminary treatment step to free the nucleic acid and/or protein components from structures or entities in which they may be contained.

13. The method of any one of claims 1 to 12, wherein prior to contacting said sample with said solid supports, the sample is subjected to a cell isolation procedure.

14. The method of claim 13, wherein one or more particular cell populations are specifically isolated.

15. The method of any one of claims 1 to 14, wherein the sample, or a cell population isolated therefrom, is subjected to a cell lysis step prior to contacting said sample with said solid supports.

16. The method of claim 15, wherein cell surface proteins of cells within or isolated from said sample are subjected to an *in vitro* modification procedure prior to the cell lysis step.

17. The method of any one of claims 1 to 16, wherein the sample is not divided at any stage of the method.

18. The method of any one of claims 12 to 16, wherein the sample is divided after cell isolation and/or lysis or after said preliminary treatment step.

19. The method of any one of claims 1 to 18, wherein said sample is contacted with said solid supports sequentially or simultaneously or in parallel.

20. The method of claim 19, wherein in a first step DNA is isolated from said sample, in a second step RNA is isolated from said sample and in a third step, protein is isolated from said sample, and wherein said steps may be performed in any order.

21. The method of any one of claims 1 to 20, wherein DNA is isolated on a support carrying surface carboxyl groups.

22. The method of any one of claims 1 to 21, wherein DNA is isolated by binding to a solid support, in the presence of a detergent.

23. The method of any one of claims 13 to 21, wherein cell lysis and nucleic acid or DNA binding to a solid support occur simultaneously or concomitantly.

24. The method of any one of claims 1 to 23, wherein RNA is isolated using an RNA-specific capture-probe carried by or attached to, or capable of binding to said solid support.

25. The method of claim 24, wherein said capture probe is or comprises a dT oligonucleotide or dU oligonucleotide.

26. The method of any one of claims 1 to 25, wherein protein is isolated using an appropriate binding partner/ligand carried by or attached to or capable of binding to said solid support.

27. The method of any one of claims 1 to 25 wherein protein is isolated using a solid support having a surface capable of effecting a chromatographic interaction.

28. The method of any one of claims 1 to 27, wherein said solid supports comprise particles.

29. The method of claim 28, wherein said particles are magnetic particles.

30. A kit for isolating nucleic acid and protein from the same sample comprising:

(a) a solid support suitable for binding nucleic acid components;

(b) a solid support suitable for binding proteins, wherein said supports of a) and b) are distinct solid supports.

31. The kit of claim 30, wherein the solid support of (a) comprises a support which is selective for binding DNA or RNA or both types of nucleic acid.

32. The kit of claim 30 or 31 wherein the kit also comprises (c) a solid support suitable for isolation of a specific cell population and/or (d) means for lysing said cells, and/or (e) a means for detecting the nucleic acid and/or protein.

33. Use of the method of any one of claims 1 to 32 for the analysis and/or comparison of mRNA and/or protein expression and/or the correlation thereof to genomic information.

Claims

1. A method of isolating nucleic acid and protein from the same sample, said method comprising contacting said sample with solid supports, wherein nucleic acid and protein components contained in said sample become bound to distinct solid supports.

2. The method of claim 1, wherein both DNA and RNA are bound to the same solid support.

3. The method of claim 1, wherein DNA and RNA are bound to distinct solid supports.

4. The method of claim 3, wherein DNA and RNA are bound to different solid supports in separate steps.

5. The method of any one of claims 1 to 4, wherein RNA and protein, or DNA and protein, or DNA, RNA and protein are isolated from the same sample.

6. The method of claim 5, wherein said RNA is mRNA.

7. The method of any one of claims 1 to 6, wherein said sample is a food or allied product, or is a clinical, environmental or biological sample.

8. The method of any one of claims 1 to 7, wherein prior to contacting said sample with said solid supports, the sample is subjected to a preliminary treatment step to free the nucleic acid and/or protein components from structures or entities in which they may be contained.

9. The method of any one of claims 1 to 8, wherein prior to contacting said sample with said solid supports, the sample is subjected to a cell isolation

procedure.

10. The method of claim 9, wherein one or more particular cell populations are specifically isolated.

11. The method of any one of claims 1 to 10, wherein the sample, or a cell population isolated therefrom, is subjected to a cell lysis step prior to contacting said sample with said solid supports.

12. The method of claim 11, wherein cell surface proteins of cells within or isolated from said sample are subjected to an *in vitro* modification procedure prior to the cell lysis step.

13. The method of any one of claims 1 to 12, wherein the sample is not divided at any stage of the method.

14. The method of any one of claims 8 to 12, wherein the sample is divided after cell isolation and/or lysis or after said preliminary treatment step.

15. The method of any one of claims 1 to 14, wherein said sample is contacted with said solid supports sequentially or simultaneously or in parallel.

16. The method of claim 15, wherein in a first step DNA is isolated from said sample, in a second step RNA is isolated from said sample and in a third step, protein is isolated from said sample, and wherein said steps may be performed in any order.

17. The method of any one of claims 1 to 16, wherein DNA is isolated on a support carrying surface carboxyl groups.

18. The method of any one of claims 1 to 17, wherein DNA is isolated by binding to a solid support, in the presence of a detergent.

19. The method of any one of claims 9 to 18, wherein cell lysis and nucleic acid or DNA binding to a solid support occur simultaneously or concomitantly.

20. The method of any one of claims 1 to 19, wherein RNA is isolated using an RNA-specific capture-probe carried by or attached to, or capable of binding to said solid support.

21. The method of claim 20, wherein said capture probe is or comprises a dT oligonucleotide or dU oligonucleotide.

22. The method of any one of claims 1 to 21, wherein protein is isolated using an appropriate binding partner/ligand carried by or attached to or capable of binding to said solid support.

23. The method of any one of claims 1 to 21 wherein protein is isolated using a solid support having a surface capable of effecting a chromatographic interaction.

24. The method of any one of claims 1 to 23, wherein said solid supports comprise particles.

25. The method of claim 24, wherein said particles are magnetic particles.

26. A kit for isolating nucleic acid and protein from the same sample comprising:

(a) a solid support suitable for binding nucleic acid components;

(b) a solid support suitable for binding proteins.

27. The kit of claim 26, wherein the solid support of (a) comprises a support which is selective for binding DNA or RNA or both types of support.

28. The kit of claim 26 or 27, wherein the kit also comprises (c) a solid support suitable for isolation of a specific cell population and/or (d) means for lysing said cells, and/or (e) a means for detecting the nucleic acid and/or protein.

29. Use of the method of any one of claims 1 to 28 for the analysis and/or comparison of mRNA and/or protein expression and/or the correlation thereof to genomic information.